hormonal use, recent surgery or trauma, advanced age, limited mobility, morbid obesity, and known thrombophilic disorder.¹

A Cochrane review of 13 RCTs including 1,774 pregnant and postpartum women, measured the effect of pharmacologic and nonpharmacologic interventions to reduce symptomatic thromboembolic events and death.² During the antenatal period, no difference was noted in symptomatic thromboembolic events between patients receiving either unfractionated heparin or low-molecular-weight heparin (LMWH) versus placebo or no treatment (2 trials, N=56; risk ratio [RR] 0.33; 95% CI, 0.04–3.0). No difference was noted in superficial or deep vein thromboses during the postnatal period between patients receiving heparin compared with placebo (1 trial, N=210; RR=0.16; 95% CI, 0.02–1.4).

A Cochrane review identified 9 RCTs including 3,358 patients and compared the use of LMWH or warfarin with placebo in patients with known malignancy receiving chemotherapy.³ LMWH reduced the occurrence of symptomatic VTE compared with placebo or no prophylaxis (6 trials, N=2,464; RR=0.62; 95% CI, 0.41–0.93; NNT 60). No difference was noted in major bleeding between the groups (5 trials, N=2,394; RR=1.6; 95% CI, 0.69–3.6). The effect of warfarin on the prevention of VTE compared with placebo was not statistically significant (1 trial, N=311; RR=0.15; 95% CI, 0.02–1.2).

A Cochrane review of 9 RCTs including 2,637 patients compared the efficacy of graduated compression stockings (GCS) in preventing the incidence of DVT among passengers flying for more than 4 hours.⁴ The use of GCS providing 15–30 mmHg of pressure decreased the incidence of asymptomatic DVT by 3.4% compared with no treatment (9 trials, N=2,637; OR 0.1; 95% CI, 0.4–0.25).

The American College of Chest Physicians issued evidenced-based guidelines for VTE prophylaxis in high-risk patients.⁵ No routine VTE prophylaxis is recommended during pregnancy or the early postnatal period in patients without additional risk factors (Grade 1B, based on RCTs with strong limitations or exceptionally strong evidence from observational studies with benefits closely balanced with risks). In outpatients with known malignancy, no routine prophylaxis with LMWH is recommended (Grade 2B, based on RCTs with strong limitations or exceptionally strong evidence from observational studies with benefits closely balanced with risks).

However, if additional risk factors are present, including prior VTE, immobilization, hormonal therapy, angiogenesis inhibitors, thalidomide use, or lenalidomide use, pharmacological prophylaxis with LMWH is recommended (Grade 2B). For high-risk patients traveling for more than 4 hours, GCS for VTE prophylaxis is recommended (Grade 2C, based on observational studies, case series, or RCTs with serious flaws or indirect evidence with uncertainty in benefits and risks). Despite evidence that the incidence of VTE among immobilized nursing home patients is similar to that of hospitalized patients, the guideline does not recommend routine VTE prophylaxis in chronically immobilized patients (Grade 2C).⁵

What is the best evaluation strategy for children with persistent lymphadenopathy?

**Evidence-Based Answer**

Evaluation of children with persistent lymphadenopathy initially requires a detailed history and physical examination. Further investigation includes baseline laboratory studies, directed specialized testing, and imaging studies. Cases remaining unexplained should undergo lymph node biopsy (SOR: B, cohort studies).

A retrospective study evaluated 457 children with persistent lymphadenopathy (>2 cm for >4 weeks’ duration) and the clinical approach to suspected malignancy.¹ Patients were divided into 3 groups according to age: <23 months (n=24, 50% male); 2–12 years (n=359, 66% male); and 12–19 years (n=74, 47% male). All patients underwent laboratory evaluation with complete blood count (CBC), peripheral smear, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), lactate dehydrogenase (LDH), uric acid, chest x-ray (CXR), throat swab cultures, serologic tests

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Evidence-Based Answer

Vitamin D supplementation probably reduces mortality and falls in men (SOR: B, extrapolated from mixed-sex meta-analyses). Higher vitamin D levels may contribute to increased physical performance in men (SOR: C, extrapolated from a mixed-sex cohort study). Routine screening for vitamin D deficiency is not recommended (SOR: B, evidence-based guideline).

A Cochrane review of 50 RCTs with more than 94,000 adult patients evaluated the effect of vitamin D on mortality. Overall mortality was reduced with vitamin D supplementation compared with placebo or no intervention (risk ratio [RR] 0.96; 95% CI, 0.93–0.99); however, women accounted for 79% of all patients.

A systematic review of 10 RCTs evaluated the effectiveness of vitamin D on fall prevention in nearly 3,000 older adults (71–90 years). Most patients were women (number not reported) and falls were reported by observation or fall diaries. Vitamin D treatment

for cytomegalovirus (CMV), rubella, toxoplasmosis, syphilis, brucella, mycobacterium tuberculosis, and human immunodeficiency virus. If necessary, an abdominal ultrasound and/or computed tomography of chest and abdomen were obtained. If malignancy was suspected then an excisional biopsy was performed.

One hundred thirty-nine excisional biopsies yielded an overall malignancy rate of 24% (111 of 457). Hodgkin's and non-Hodgkin's lymphoma were the most frequently found (83%, 93 of 111 cases), and malignancy was most common in the 12- to 19-year-old group (55%, 74 of the 134 teenagers). Biopsy yielded a specific identifiable etiology for only 39% of the benign group with infectious mononucleosis and acute lymphadenitis, the most frequent causes for persistent lymphadenopathy.¹

A prospective study looked at 116 children (mean age, 7 years) with persistent lymphadenopathy, evaluating them with an algorithm (TABLE) in an outpatient setting. Overall, 62% of the patients' conditions were identified using this algorithm.

Of those patients diagnosed, 88% were diagnosed by the third step of the algorithm. Infectious lymphadenopathy was the most common etiology (61%). Thirty-three percent of patients underwent biopsy, and neoplastic lymphadenopathy was discovered in 10% of this group of children, with the remainder having no diagnosis.²

A retrospective study looked at referral patterns of family physicians for 82 patients who underwent biopsy for unexplained lymphadenopathy. The algorithm used the history with the initial work-up with a CBC and differential count, ESR, CRP, LDH, throat culture, CXR, antinuclear antibody (ANA), and Mantoux skin test (PPD).

Investigators found that up to 98% of patients required no referral. Children with an inconclusive diagnosis were evaluated with additional serologic testing to include Epstein Barr virus, hepatitis virus, salmonella, toxoplasmosis, and CMV.³

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The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Army Medical Department, the Army at large, or the Department of Defense.